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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,119	04/13/2007	Timothy Charles Ramsey Prickett	36697.17	1813

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,119	PRICKETT ET AL.	
	Examiner	Art Unit	
	JAMES L. GRUN	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-36 remain in the case.

The disclosure is objected to because of the following informalities: the brief description of all multi-panel drawings (Figs. 5A-5C, 6A-6B, 9A-9D, 11A-11B, 12A-12D), and all reference to such drawings in the specification must indicate the panel of the Figure which is described or to which the reader is being referred, e.g. the Figures should be described and cited as Figure 6A or 6B, or Figure 5A or 5B or 5C. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-4, 6-19, and 21-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, particularly the invention commensurate in scope with these claims.

Applicant's specification, while describing and being enabling for determination of skeletal development in pre-adults, and in those suspected of having a skeletal disease or disorder, with determinations of the N-terminal fragment of pro-C-type natriuretic peptide (NT-proCNP) in plasma, does not reasonably provide description or enablement for determinations indicative of skeletal disease or disorder in subjects with biological samples generally. As taught in Prickett et al. (Biochem. Biophys. Res. Comm. 286: 513, 2001) the level of the peptide fragment is elevated in adults with congestive heart failure and the detection of an elevated level in such a patient population would not be indicative of skeletal disease or disorder. It would also seem that the levels of the peptide fragment in a sample such as brain or stool may not reflect the status of the skeleton in a subject. Thus, absent further written description and guidance from applicant, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 1-8, 11, 12, 14-21, 24, 25, 28-34, and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for anti-NT-proCNP antibodies for use in immunoassays, does not reasonably provide written description or enablement for a method or binding means generally, and in particular for a receptor specific for NT-proCNP. Applicant teaches only immunoassay detection of the fragment. Absent further written description and guidance from applicant, one would not know or be able to predict what other "receptors" specifically bind to the NT-proCNP fragment or subsequences thereof and predictably function in the assay or kit to detect NT-proCNP other than specific antibodies. To

provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics when coupled with a known or disclosed structure/function correlation, methods of making the claimed product, or any combination thereof. The specification does not provide sufficient recitation of distinguishing identifying characteristics of the genus of binding agents, means, or "receptors" other than for antibody populations specific for NT-proCNP which predictably function in the assay or kit to detect NT-proCNP. Absent further written description and guidance from applicant, one would not know or be able to predict what other method functions to specifically detect the peptide fragment other than an immunoassay with the specific antibodies. Thus, the specification does not provide sufficient written description to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, "the" level or mean lack antecedent basis. In these claims, it is believed --wherein-- was intended.

In claim 13, "using" is not a valid method step, --with-- is suggested.

In claim 14 and claims dependent thereupon, "the" skeletal growth, level, or mean lack antecedent basis.

In claim 15, "the" skeletal age, level, or mean lack antecedent basis.

In claim 16 and claims dependent thereupon, "the" level or mean lack antecedent basis.

In claim 18, it is believed --pre-adult-- was intended.

In claims 26 and 27, "using" is not a valid method step, --with-- is suggested. In claim 27, "the" specific disease lacks antecedent basis.

In claim 29 and claims dependent thereupon, recitations of "the" level or rate lack antecedent basis.

In claims 31 and 32, "the" administration lacks antecedent basis.

In claim 33 and claims dependent thereupon, recitations of "the" level lack antecedent basis.

In claim 36, it is not clear what applicant intends as encompassed by "proCNP(1750)."

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6-9, 11-17, 21, 22, 24-28, 33, 34, and 36 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Prickett et al. (Biochem. Biophys. Res. Comm. 286: 513, 2001).

Prickett et al. teach the detection and measurement of the N-terminal fragment of pro-C-type natriuretic peptide (NT-proCNP) in human plasma. Measurement was performed with a competitive immunoassay method with antibodies specific for a 15 amino acid peptide corresponding to the N-terminal sequence of the proCNP peptide (see e.g. pages 513-514). The antibodies were immobilized by an anti-immunoglobulin antibody in the method. Levels in the plasma of subjects were compared to levels in normals (see e.g. Fig. 4). The reference suggests that the circulating fragment is derived from endothelium and bone and that measurement of the fragment may reflect CNP secretion/activity in these tissues in normal and diseased states (see page 517). It is noted that a clause merely reciting a desired result of a positively recited process step is not given weight.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-36 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Prickett et al. (Biochem. Biophys. Res. Comm. 286: 513, 2001) in view of Buechler (US 2003/0219734),

Yasoda et al. (J. Bone Min. Res. 15(Suppl. 1): S243, 2000), and Chusho et al. (Proc. Natl. Acad. Sci. USA 98: 4016, 2001).

The teachings of Prickett et al. are as set forth previously in this Office action and differ from the invention as instantly claimed in not teaching monoclonal antibodies specific for NT-proCNP and in not specifically exemplifying determinations in patients with suspected skeletal diseases.

Buechler teaches elicitation of antibodies, polyclonal, monoclonal, recombinant, or antigen-binding fragments thereof, to peptide fragments of C-type natriuretic peptide comprising at least 6 contiguous amino acids for assays, such as sandwich immunoassays in which a first antibody is bound to a solid surface, for determination of the peptide fragments in a sample, such as blood, serum, or plasma (see e.g. pages 3-7).

Yasoda et al. teach skeletal overgrowth in transgenic mice that overexpress C-type natriuretic peptide and Chusho et al. teach dwarfism in knockout mice lacking C-type natriuretic peptide expression.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to have substituted monoclonal antibodies and alternative assay formats such as sandwich immunoassays, as taught in Buechler, for the polyclonal antibodies and competitive assay in Prickett et al. because to do so is notoriously old and well known in the art. It would have been obvious to have generated monoclonal antibodies in order to provide a potentially unlimited source of homogeneous reagent specific for defined epitopes of the peptide in order to detect particular fragments of C-type natriuretic peptide as taught in Buechler. It would have been further obvious to have measured the NT-proCNP fragment in plasma samples

from patients with active bone growth as a reflection of CNP secretion/activity in bone in normal and diseased states with the method of Prickett et al., as modified, because to do so is specifically suggested in Prickett et al. One would have had a reasonable expectation of success in determining differences in normal and diseased bone states with the method of Prickett et al., as modified, in view of the teachings of Yasoda et al. and Chusho et al. regarding the participation of C-type natriuretic peptide in bone development.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Woloszczuk et al. (WO 01/14885) teach antibodies and immunoassays for the detection and measurement of the N-terminal fragment of pro-C-type natriuretic peptide (NT-proCNP).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/J. L. G./
James L. Grun, Ph.D.
Examiner, Art Unit 1641
June 25, 2008

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641